

Predictors of maternal and fetal outcome in severely anemic pregnant mothers: A sequential mixed methods study

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ABSTRACT

Introduction: Severe anemia in pregnancy increases maternal and neonatal morbidity and mortality in the antenatal period. **Objective:** To find out the maternal and fetal outcomes in severely anemic pregnant women and explore the reason for the persistence of severe anemia in pregnant women. **Materials and Methods:** Sequential explanatory mixed method study (Quan-Qual) was conducted in the Government Women and Children Hospital for a period of 1 and half years. Most of the people were from rural backgrounds and belonging to low socioeconomic status have been registered. Quantitative data were collected from 125 severe anemic cases; a consecutive sampling technique was applied. In-depth interviews were conducted among purposively selected severe anemic patients ($n = 15$) who were vocal and willing to explore the reason for the persistence of anemia. The interviews were conducted till the point of saturation. Ethical principles were adhered throughout the study. Quantitative data were analyzed using SPSS software. Manual content analysis was done for qualitative data. **Results:** Among 125 severe anemic patients, 12.8% patients had preterm labour, about 23.2% had inadequate lactation, and 13.6% had a puerperal febrile illness. It was found 41.6% of neonates had respiratory distress and 33.6% had the refusal of feeds. When compared to vaginal delivery, women undergoing cesarean section have 3.2 times (95% confidence interval 1.39-7.32) higher odds of developing maternal complications. Nagelkerke's R^2 value for the model was 11.1%. Five broad categories namely Family centric nature, Lack of awareness, Pill burden, Food Fads, and Myths related to iron intake emerged from the study. **Conclusion:** Complications can occur in mothers and neonates if anemia is not corrected in early trimester.

Keywords: Anemia, IDI, neonatal morbidity, sequential mixed method

Introduction

Anemia is the most common medical disorder in pregnancy and has a varied prevalence, etiology, and degree of severity in

different populations and it is more common in nonindustrial countries. As per the World Health Organization's (WHO) definition hemoglobin concentration of less than 11 g/dL (7.5 mmol/L) and a hematocrit of less than 0.332 is considered anemia in pregnancy. The WHO uses the following hemoglobin cut-offs to define the severity of anemia in pregnant women, 100 to 109 g/L as mild anemia, 70 to 99 g/L as moderate anemia, and less than 70 g/L for severe anemia.^[1] In India, more than 90% of anemia cases are estimated to be due to iron deficiency because high iron requirements during pregnancy are not easily

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fulfilled by dietary intake especially when iron bio-availability is poor.^[1]

Iron deficiency anemia is a major public health nutritional problem affecting all ages. Across the globe, 1.62 billion people are anemic (24.8%) and among pregnant women 41.8% are anemic. India has one of the highest prevalences of anemia (74.3%) in the world in the general population and more than half (56%) of the pregnant women are anemic in developing countries including India. In the country, the major etiological factors responsible for anemia during pregnancy can be attributed to poor dietary iron consumption and low iron bioavailability in the Indian diet. Moreover, blood loss due to malarial infection, hookworm infestation, and vitamin B12 deficiency make the situation dismal. Maternal anemia is one of the important factors which determines the pregnancy outcome and is responsible for the increased incidence of premature births, low birth weight, and high perinatal mortality.^[2] Iron deficiency, which results from a protracted negative iron balance and accounts for 50% of anemia in women worldwide, is the primary cause of anemia in women of reproductive age worldwide.^[3] WHO statistical data show that 25% of maternal deaths occur due to postpartum hemorrhage and it was significantly associated with the varying degree of severity of anemia. Pregnant women with moderate-to-severe anemia had a significantly greater total blood loss of an average of 91 mL as compared to nonanemic women.^[4,5]

Anemia is also related to poor neonatal outcomes, such as preterm delivery, low birth weight, low Apgar scores, and intrauterine fetal death.^[4] Despite various actions taken by the government to counteract anemia from adolescents age through Weekly Iron and Folic acid and providing free iron tablet supply during pregnancy still there is a rise in severe anemia causing an increase in maternal and neonatal morbidity and mortality in the antenatal period. We faced a similar situation in our outpatient department, where the prevalence of anemia especially severe anemia in antenatal mothers was high. Hence, we decided to conduct the study with the following objectives to find out the maternal and fetal outcome in severely anemic pregnant women and its associated factors and to explore the reason for the persistence of severe anemia in pregnant women.

Materials and Methods

Study settings and study design

The present sequential explanatory mixed method study (Quan-Qual) was conducted in the Government Women and Children Hospital, for a period of 1 and half years from January 2018 to August 2019. Free medical services and care are provided to all antenatal case (ANC), postnatal case, mothers, and children. Most of the people from rural backgrounds and belonging to low socioeconomic status register here for ANC care and free institutional delivery.

Sample size and sampling

Quan: The sample size was calculated based on the proportion of severe anemia as recorded in Medical Record Statistics using

this formula $N = (z_{1-4})^2 p (1-p) / d^2$, where p is the anticipated proportion of severe anemia 5.54% with 5% absolute precision sample size was calculated to be 81. Considering the 20% nonresponse rate, the final sample size was 97. Finally, we included all the severe anemia cases during the study period which was 125. A consecutive sampling technique was applied.

Qual: In-depth interviews (IDI)^[6] were conducted among purposively selected severe anemic patients ($n = 15$) who were vocal and willing to explore the reason for the persistence of anemia. The interviews were conducted till the point of saturation.

Study participants

All the antenatal mothers attending the above hospital fulfilling the inclusion criteria ($n = 125$) were included in the study after obtaining written, informed, valid consent.

Inclusion criteria: All third-trimester antenatal mothers with any parity with Hb% <10 gm%, belonging to >18 years, and those who are vocal and willing to participate in the study were included.

Exclusion criteria: Pregnant women in the first and third trimester with Hb \geq 10 gm. Women with known medical disorders such as diabetes mellitus, chronic hypertension, cardiac or endocrine disorders, and surgical conditions were excluded from the study.

Data collection

After obtaining institutional ethical clearance and written informed consent, the data were collected by using a pretested semi-structured questionnaire which comprised sociodemographic details, clinical examination, and reports of blood. Apart from the general physical examination which comprised of history and examination for thyroid, breast, and abdominal examination. Presenting complaints (labor pains, leaking per vaginum, and bleeding per vaginum) history of presenting illness, menstrual history (LMP, age at menarche, duration and length of cycles, and blood loss), obstetric history (gravida, parity, and no. of live issues), past medical and surgical history, and family history will be noted. General examination including height, weight, pallor, pedal edema, vitals-pulse rate, blood pressure systemic examinations-cardiovascular examination, respiratory system will be noted. Per abdominal (P/A) examination, local examination, and per vaginal (P/V) examination were also done.

Face-to-face interviews were conducted among the participants after obtaining informed written consent using a semi-structured interview guide. Ethical principles have been followed throughout the conduct of the study. IDIs were conducted in Tamil by trained qualitative researchers. Interviews were audio-recorded with participants' permission and each IDI lasted for 23-40 minutes (the average duration was 32 minutes). To ensure participant validation debriefing was done before closing the interview, they were asked if they wanted to add any extra information. A total of 15 participants were interviewed until data saturation was obtained.

Analysis of data

Quantitative: All the data were entered into Microsoft Excel 2010 and were analyzed using SPSS Software version 23.0. Discrete variables were presented as frequency and percentage and continuous variables as mean and standard deviation. Logistic regression was performed to find out the association between socio-demographic variables and maternal and fetal complications in severely anemic mothers. A *P* value of <.05 was fixed as a significant level.

Qualitative: Audio recordings were transcribed in English. Transcripts were proofread and edited beforehand and were thoroughly read. Inductive coding of the transcripts was done manually by two qualitative researchers for better interpretation. Codes obtained from the transcript were merged to form categories, subthemes, and themes. To increase the internal validity, the results were reviewed by another faculty trained in qualitative research who is not part of the study. Statements in italics indicate direct statements from participants. "Consolidation criteria for reporting qualitative research" guidelines were used for reporting the findings.^[7]

Ethics issues

Institutional Research and Ethics Committee clearance were obtained (EC No. GHIEC/2017). Ethical principles such as respect for the persons, beneficence, justice, and ensuring confidentiality were adhered to, throughout the study. Informed written consent was obtained from all participants.

Results

Table 1 showed that 12.8% of patients had preterm labor, about 23.2% had inadequate lactation and 13.6% had a puerperal febrile illness.

Table 2 shows 41.6% had respiratory distress, 33.6% had refusal of feeds, and 24.8% had lethargy.

Binomial logistic regression was performed to ascertain the effects of age, body mass index, Hb%, mean corpuscular volume

(MCV), gravida, and mode of delivery of severely anemic women on the likelihood of development of maternal complications. Of six predictors, only one was statistically significant: The cesarean section. When compared to vaginal delivery, women undergoing cesarean section have 3.2 times (95% confidence interval [CI], 1.39-7.32) higher odds of developing maternal complications. Nagelkerke's *R*² value for the model was 11.1%. Binomial logistic regression was done to find out the maternal factors associated with fetal complications in severely anemic women. Of six predictors included in the analysis (age, body mass index, Hb%, MCV, gravida, and mode of delivery), only two (gravida and mode of delivery) were found to be statistically significant. Multigravidas when compared with primi gravidas had 0.28 times (95% CI; 0.11-0.71) lower risk of developing fetal complications. Women undergoing cesarean section had 2.61 times higher odds of developing fetal complications when compared with those women who had a vaginal delivery. Nagelkerke's *R*² value for the model is 24.1% [Table 3].

Table 4 five broad categories emerged from IDI namely Family centric nature (eating food after everyone eats in the family), Lack of awareness, Pill burden (*red colored tablet (iron) give me metallic taste*), Food Fads (avoid taking green leafy vegetables), and Myths related to iron intake (*iron tablet will lead to decrease the color of the newborn*) emerged from the study.

Discussion

Key findings of the study

In the present study it was found that 12.8% of patients had preterm labor, about 23.2% had inadequate lactation, and 13.6% had puerperal febrile illness. Considering the fetal complication, 41.6% had respiratory distress, 33.6% had refusal of feeds, and 24.8% had lethargy. The risk of preterm birth, LBW, and stillbirth was higher in anemic women and increased with the severity of anemia. LBW is highly correlated with gestational age at delivery and both are also correlated with other pregnancy complications such as pre-eclampsia.^[8]

In this present study when compared to vaginal delivery, women undergoing cesarean section have 3.2 times (95% CI; 1.39-7.32) higher odds of developing maternal complications. Nagelkerke's *R*² value for the model was 11.1%; this may be due to the fact the double the blood loss (1 liter) in C-section when compared to SVD (500 mL) which still worsens the severe anemic condition.

Table 1: Maternal complications in severely anemic pregnant women

Complications	Frequency (n)	Percentage (%)
Preterm Labour	16	12.8
Inadequate Lactation	29	23.2
Puerperal Febrile Illness	17	13.6
Episiotomy Site Infection	13	10.4
Surgical Site Infection	12	9.6
Preeclampsia	8	6.4
Surgical Wound Dehiscence	7	5.6
PPH	4	3.2
Abruption Placenta	3	2.4
Placenta Previa	2	1.6
Cardiac Failure	0	0
Mortality	0	0

PPH: Postpartum hemorrhage

Table 2: Fetal complications in severely anemic pregnant women

Complication	Frequency (n)	Percentage (%)
Meconium stained liquor	15	12
Respiratory distress	52	41.6
Seizures	14	11.2
Lethargy	31	24.8
Refusal of feeds	42	33.6
Congenital anomalies (B/L CTEV)	2	1.6

Table 3: Factors associated with maternal complications in severely anemic pregnant women (N=125)

Variables	B	Sig	Crude OR with 95% CI	Adjusted OR with 95% CI
Age	0.04	0.45	1.05 (0.96-1.14)	1.04 (0.94-1.15)
BMI	0.05	0.47	1.02 (0.91-1.14)	1.05 (0.92-1.19)
Hb%	-0.04	0.88	0.94 (0.56-1.67)	0.96 (0.53-1.72)
MCV	-0.04	0.23	0.97 (0.91-1.02)	0.96 (0.91-1.02)
Gravida (Ref-Primi)				
Multi	-0.22	0.61	0.96 (0.47-1.96)	0.81 (0.35-1.87)
Mode of delivery (Ref-Vaginal delivery)				
Caesorean section	1.16	0.006	3.21 (1.43-7.21)*	3.20 (1.39-7.32)*

CI = Confidence Interval; *P value < 0.05

Pregnancy itself leads to anemia causing a state of hydraemic plethora where there is a disproportionate increase of plasma volume as compared to red blood cell mass leading to an apparent reduction of red blood cells, haemoglobin, and hematocrit values. The dilution picture is normocytic and normochromic which is so called physiological anemia of pregnancy.^[9] This physiological anemia is further complicated by acquired nutritional deficiencies of iron, folic acid, vitamin B12, and other factors namely hemolytic or hemorrhagic conditions due to acute or chronic blood loss.

Iron needs exhibit a marked increase during the second and especially during the third trimesters when median daily needs increase up to an average of 5.6 mg per day (i.e. 4.1 mg above median prepregnancy needs). The approximate range would be 3.54 and 8.80 mg per day. Food iron cannot meet this amount of absorbed iron needs even if iron fortification is in place. Iron-deficient anemic women have shorter pregnancies than nonanemic or even anemic but not iron-deficient pregnant women. Iron deficiency anemia results in impaired transport of hemoglobin and thus oxygen to the uterus, placenta, and fetus. It also causes tissue enzyme and cellular dysfunction. This mechanism can explain impaired myometrial contractility resulting in an atonic uterus, as well as placental dysfunction leading to preterm birth, low birth weight, growth-restricted babies, and perinatal deaths. Reduced oxygen delivery can also result in impaired wound healing.^[10] Severe anemia is a pregnancy complication that can be prevented easily and fetomaternal complications related to anemia can be preventable. The major causative factor is iron deficiency anemia, which increases the risk of low birth weight and intrauterine growth restriction.^[11]

Some studies have demonstrated that women with less hemoglobin values had babies with low birth weight than women with higher hemoglobin values, but there had not been exclusion of other factors which might have contributed to low birth weight and severity of anemia.^[12] In India, it is common to see patients with severe anemia late in pregnancy with no prior antenatal visits, especially in low economic settings. Severity of anemia is an independent risk factor for LBW and pre-eclampsia.

Table 4: IDI to explore reasons for severe anemia in pregnancy

Categories	Codes
Family centric nature	Women generally prioritize the health and wellbeing of family members and neglect their own nutrition and health <i>"Generally we eat food after everyone eats in the family, sometime there will be no vegetables leftover"</i> <i>"Similarly weekly once we used to cook non-veg, in the end only one piece will be left over"</i> <i>"As it was my second pregnancy nobody bothered about me whether I eat or not, even for health checkups I used to go on my own"</i> <i>"To decrease the family burden I got married very early at 17 years I was not prepared for marriage and I got pregnant very soon I didn't know the importance of nutrition"</i>
Lack of awareness	Lack of awareness among women about the importance of iron and folic acid intake during pregnancy <i>"I have not taken any tablets related to iron before pregnancy, I felt unnecessary tablets are not good for health"</i> <i>"I didn't have awareness of the importance of taking tablets (folic acid) before conceiving the baby"</i> <i>"Sometimes I have also avoided tablets to remove worms (albendazole) and iron tablets which they gave me in government hospital"</i>
Pill burden	Women reported not liking the taste and size of iron tablets. They also hate the idea of taking it regularly, since they fear it might cause side effects <i>"Taking that red-colored tablet (iron) gives me a metallic taste which causes vomiting most of the time"</i> <i>"the size of the tablet is also big"</i>
Food Fads	Many women avoid certain food items, especially during pregnancy and childbirth and unfortunately, most of these foods have rich iron content, which might have helped them in improving their anemia. <i>"In pregnancy, I dint like to take nonveg and green leafy vegetables as it causes nausea"</i> <i>"from childhood, I used to avoid taking green leafy vegetables"</i>

Reason for severe anemia

The cause of severe anemia is not acute; it is multifactorial and has been persistent for a long period. "Emic" perspective of the patient clearly explains the reason. In a country like India, the various cultural aspects like eating leftover food after all the family members eat, lead to nutritional impairment. The vicious cycle tends to transfer for generations. The lack of family support. Although the government has laid down various measures to tackle this problem through initiatives like Weekly Iron and Folic acid for school-age group, Bi-annual deworming proper supervision is not done as they do not cherish importance. Diet diversity is another reason as none of the participants told they frequently take fruits and nonveg and they only take seasonal vegetables which are affordable. None of the participants had awareness of preconceptional folic acid as it does not lead to neural tube defects but can also counter anemia which is a point to consider. In developing countries, anemia in its severe form in pregnant women remains one of the most intractable public health problems in developing countries because of various socio-cultural problems including illiteracy, poverty, lack of awareness, cultural and religious taboos, poor dietary habits, and high prevalence of parasitic infestation.^[13]

According to ICMR, the relative prevalence of mild, moderate, and severe anemia are 13%, 57%, and 12%, respectively, in India. The frequency of anemia during pregnancy depends primarily on pre-existing iron states and prenatal supplementation. It is more common among indigent women and is influenced by dietary customs.^[14] The role of adequate diet and optimal pre-pregnancy nutritional status needs to be emphasized in women of childbearing age, particularly since pregnancy may be too short a period of time in which to reduce pre-existing anemia.^[15,16]

Premature births are more common in women with moderate anemia. They deliver infants with lower birth weight and perinatal mortality is higher in these babies. The cardiac output is raised even at rest, the stroke volume is larger, and the heart rate is increased. Palpitation and breathlessness even at rest are symptoms of these changes. These compensatory mechanisms are inadequate to deal with the decrease in Hb levels.^[17]

The management of anemia depends upon the severity of the condition and the duration of pregnancy. In early pregnancy, even severe iron deficiency anemia is manageable by high doses of oral iron. In severe anemia and in cases of malabsorption or noncompliance, parenteral iron therapy may be recommended. In moderate to severe anemia close to term blood transfusion may have to be considered.^[10]

Strength and limitations

Qualitative in-depth exploration (Emic perspective) from severe anemic patients by trained qualitative researchers adds to the validity of the study. The first and second trimester patients could have been included in the study so that we would have got a good sample size but unfortunately, most of the patients paid their first visit was only the mid-late third trimester. In our study, the outcome was affected by cofactors like socio-economic status and poor nutrition which could not be eliminated because anemia and poor nutrition often coexist and contributes to maternal disorders that lead to poor maternal and fetal outcome. Being hospital-based study with a small sample size, the results of the study may not be generalized.

Conclusion

From the present study, it is clear that complications can occur in mother and neonates if anemia is not corrected in early trimester. Nutritional anemia was most likely caused in the present study as the patients who came early showed improvement in maternal and fetal outcome with treatment. Lower the hemoglobin, greater was the incidence of lower birth weight, preterm labor, and puerperal complications.

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Conflicts of interest

There are no conflicts of interest.

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